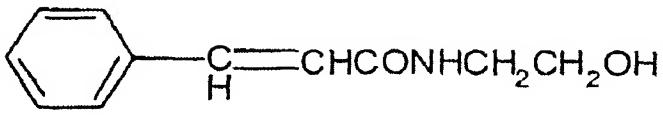
SUPPORT FOR THE AMENDMENTS

Claim 27 is amended to use structure and wording consistent with U.S. patent law practice.

REMARKS/ARGUMENTS

The claimed invention provides a method for treating rosacea by topical application of a dermatological composition containing idrocilamide. The chemical structure of idrocilamide is shown below:



The chemical name of idrocilamide is N-(2-hydroxyethyl)cinnamide. Applicants have described rosacea as follows (page 1, lines 8-15):

> Rosacea is a common, chronic and progressive inflammatory dermatitis associated with vascular instability. It mainly affects the central part of the face and is characterized by redness of the face or hot flushes, facial erythema, papules, pustules and telangiectasia. In serious cases, especially in men, the soft tissue of the nose may swell and produce a bulbous swelling known as rhinophyma.

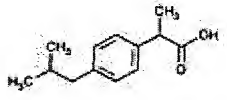
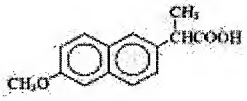
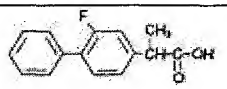
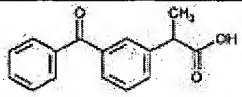
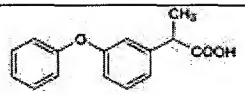
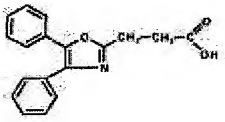
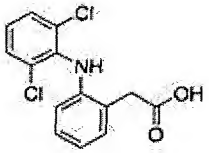
The rejection of Claims 16-31 under 35 U.S.C. 103(a) over Arkin et al. (WO 02/074290) in view of Barnwarth et al. (Tissue and systemic diffusion of idrocilamide after cutaneous administration) is respectfully traversed.

Arkin describes a topical preparation for treatment of rosacea which contains a non-steroidal anti-inflammatory drug classified according to chemical structure (page 4, lines 5-15) as follows:

> - Salicylic acid derivatives (e.g., aspirin, sodium salicylate, choline magnesium trislicylate, diflunisal, salicylsalicyclic acid, sulfasalazine, olsalazine)

- Para-aminophenol derivatives (e.g., acetaminophen)
- Indole and indole acetic acids (e.g., indomethacin, sulindac, etodolac)
- Aryl acetic acids (e.g., tolmetin, diclofenac, ketorolac)
- Arylpropionic acids (e.g., ibuprofen, naproxen, flubiprofen,ketoprofen, fenoprofen, oxaprozin)
- Anthranilic acids (fenamates) (e.g. mefanamic acid, meclofenamic acid);
- Enolic acids (e.g., oxicams (piroxicam, tenoxicam), pyrazolidinediones (phenylbutazone, oxyphenthratazone)
- Alkanones (e.g., nabumetone).

Applicants provide the structures of the Arylpropionic acids listed above for reference purposes in the following table.

Arylpropionic acid	Structure
Ibuprofen	
Naproxen	
Flurbiprofen	
Ketoprofen	
Fenoprofen	
Oxaprozin	
Dicyclofenac	

In the table the structure of Dicyclofenac is also provided for later discussion. Comparison of the structure of idrocilamide with the arylpropionic acids listed by Arkin shows that the former is an 2,3 unsaturated arylamide having no free carboxyl group, while all the Arkin structures are carboxylic acids having no 2,3 unsaturation.

The Office acknowledges that Arkin does not expressly teach the inclusion of idrocilamide (Official Action dated September 29, 2009, page 7, last line) and cites Bannwarth to show this compound.

Bannwarth describes a study of the tissue and systemic distribution of idrocilamide in patients suffering from chronic arthropathy of the knee (page 2, lines 8-10; English translation). The study indicates that following topical application, the idrocilamide moves via percutaneous diffusion and systemic passage into the underlying articular and para-articular elements of the knee, i.e., it passes through the dermis and migrates into interior tissues and fluids. Bannwarth states (page 7, lines 11-15):

> . . ., the physicochemical characteristics of idrocilamide (molecular weight less than 200 and amphiphilic nature with lipophilic predominance) favor its passage through the epidermis. . . ., the distribution is continued towards the deepest layers to the joint capsule and the synovial membrane.

Bannwarth further describes that the data obtained in his study shows that the idrocilamide which appears in the synovial fluid originates more from blood flow than from direct diffusion from the skin and notes that a similar observation had been made with diclofenac gel (page 8, lines 12-14).

The Office has alleged that based on motivation provided by the Bannwarth reference, it would have been obvious to one of ordinary skill in the art at the time of the invention to include idrocilamide in the invention of Arkin (Official Action dated September 29, 2009, page 8, lines 7-11).

Applicants note that in reversing an obviousness rejection in *Ex parte* SUSUMU TANAKA and YASUO MURAKAMI (Appeal 2007-3845; Decided: March 28, 2008) the Board of Patent Appeals and Interferences stated:

> In order to establish a prima facie case of obviousness, the Examiner must show that each and every limitation of the claim is described or suggested by the prior art or would have been obvious based on the knowledge of those of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988). "[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)

Applicants respectfully submit that the apparent reasoning of the Office in support of the prima facie obviousness is critically flawed. Firstly, Bannwarth only describes a similarity in that both diclofenac and idrocilamide show higher concentrations in the plasma than in the synovial fluid of the knee. The reference makes no statement regarding the relative performance of the two substances regarding analgesic effect and therefore cannot be cited as showing the two compounds as being functionally equivalent.

Moreover, Bannwarth describes distribution in the working parts of the knee which are much deeper than the epidermal layer which is targeted in the claimed invention and in the Arkin description. Applicants submit that as Bannwarth clearly describes the passage of idrocilamide through the dermal layer and into the structure of the knee, it actually provides motivation that would teach away from an application requiring an effect in the epidermal layer as directed to treatment of inflammatory dermatitis.

Furthermore, comparison of the chemical structures of the arylpropionic acids described by Arkin to idrocilamide shows such significant structural dissimilarities, that Applicants respectfully submit, that one of ordinary skill in the art would not consider idrocilamide to be of the same chemical family and would not therefore predict similar chemical or functional properties. As indicated, idrocilamide has no carboxyl group, is a

carboxamide and has unsaturation in the 2 position of the carbon chain. In contrast, the arylpropionic acids described by Arkin are carboxylic acids, have no 2-3 unsaturation and no carboxamide group. Applicants respectfully submit that the described structural differences are significant and therefore one of ordinary skill in the art could not predict the relative performance of these compounds in any application without more information.

In view of all the above, Applicants respectfully submit that the Office has not met the burden necessary to support a conclusion of obviousness based on the cited references. The Office has not provided a rational explanation as to why one of ordinary skill in the art would be motivated by the description of Bannwarth to employ idrocilamide for the treatment of rosacea as described by Arkin. The two references are directed to two different areas of treatment as well as two different ailments.

Accordingly, Applicants respectfully request that the rejection of Claims 16-31 under 35 U.S.C. 103(a) over Arkin in view of Barnwarth be withdrawn.

The rejections of Claims 25 and 31 under 35 U.S.C. 112, first paragraph, is respectfully traversed.

Applicants note the M.P.E.P. § 2163 II. 2. states:

> Information which is well known in the art need not be described in detail in the specification. See e.g., *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986)

The Office has pointed to the recitation of "cosmetic active agent," "skin calmative and protective agents" and "pro-penetrating agents" as failing to comply with the written description requirement. Applicants respectfully submit that these terms are known in the art and that one of ordinary skill would recognize the meaning and substance of Applicants description.

Applicants respectfully note that the claimed invention is directed to a method for treating rosacea comprising applying topically to skin a pharmaceutical composition comprising idrocilamide. Rosacea as described above is associated with the facial skin tissue.

Therefore, known skin-care products such as described in the description of Skin-Care Products and Anti-acne Preparations in Kirk-Othmer Encyclopedia of Chemical Technology, Fifth Edition, Vol. 7, pp 842-844 (copy attached), would be recognized as cosmetic active agents according to the claimed invention.

Applicants point to page 6, lines 36-37, which state in pertinent part:

> . . .skin calmative and protective agents **such as allantoin** . . .

Applicants submit that the description of allantoin as a skin calmative and protective agent conveys an understanding to one of ordinary skill in the art of the meaning of skin calmative and protective agent. A description of allantoin as a skin care product is attached. Applicants note that this material is an extract from the roots and leaves of the comfrey plant.

Applicants respectfully point to U.S. 7,316,810, Col. 4, lines 45-52, which describes propenetrating agents as follows:

> The propenetrating agent, which makes it possible to facilitate the penetration of the active principles, preferably dissolves the active principle present in the composition according to the invention. More particularly, it is chosen from volatile $C_1 - C_4$ alcohols, such as ethanol or isopropanol, from polyhydric alcohols, such as propylene glycol, and from glycol ethers such as ethoxydiglycol.

Applicants respectfully submit that in view of the above, Claims 25 and 31 do comply with the written description requirement. Accordingly, Applicants respectfully request that the rejections of Claims 25 and 31 under 35 U.S.C. 112, first paragraph, be withdrawn.

The rejections of Claim 29 under 35 U.S.C. 112, first paragraph, is respectfully traversed.

An immunosuppressive agent is a medication that slows or halts immune system activity. Immunosuppressive agents may be given to prevent the body from mounting an immune response after an organ transplant or for treating a disease that is caused by an overactive immune system.

Applicants herewith submit a listing of known immunosuppressive agents (encyclopedia of medical concepts) and respectfully submit that such clear definition clearly complies with the written description requirement.

Applicants submit that anti-proliferative agents are related to « Chemotherapy " which is treatment of cancer with anticancer drugs. Chemotherapy drugs are classified based on how they work. The main types of chemotherapy drugs are described below:

· Alkylating drugs kill cancer cells by directly attacking DNA, the genetic material of the genes. Cyclophosphamide is an alkylating drug.

· Antimetabolites interfere with the production of DNA and keep cells from growing and multiplying. An example of an antimetabolite is 5-fluorouracil (5-FU).

· Antitumor antibiotics are made from natural substances such as fungi in the soil. They interfere with important cell functions, including production of DNA and cell proteins. Doxorubicin and bleomycin belong to this group of chemotherapy drugs.

· Plant alkaloids prevent cells from dividing normally. Vinblastine and vincristine are plant alkaloids obtained from the periwinkle plant.

· Steroid hormones slow the growth of some cancers that depend on hormones. For example, tamoxifen is used to treat breast cancers that depend on the hormone estrogen for growth.

Applicants respectfully submit that in view of the above, Claim 29 does comply with the written description requirement. Accordingly, Applicants respectfully request that the rejections of Claim29 under 35 U.S.C. 112, first paragraph, be withdrawn.

Applicants respectfully request that the provisional rejection of Claim 30 on the ground of nonstatutory obviousness-type double patenting over Claims 19-29 of copending Application No. 10/590031 be held in abeyance pending identification of patentable subject matter in the above-identified application.

Applicants respectfully submit that the above-identified application is now in condition for allowance, pending resolution of the provisional rejection of Claim 30 on the ground of nonstatutory obviousness-type double patenting and early notice of such status is earnestly solicited.

Respectfully submitted,

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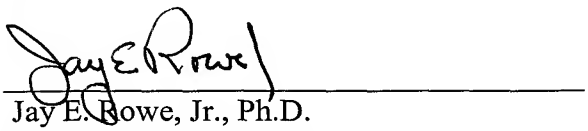
MAIER & NEUSTADT, L.L.P.
Norman F. Oblon



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